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Filed: November 26, 1991

35. An isolated DNA sequence comprising the nucleotide sequence of
ATCC #75011.

REMARKS

Reconsideration of the application and entry of the amendments
is requested.

The following documents accompany this response:

1. Appendix A - Claims
2. Information Disclosure Statement, PTO Form 1449, required
fee and references.
3. Petition for Extension of Time and Required Fee
4. Deposit Declaration

The Draftsman's Drawing Review has been noted. In accordance
with 37 CFR 1.85, Applicants will submit corrected formal drawings
upon notification of allowance of claims in the present
application.

Applicants have requested a certified copy of PCT/US91/03388
for which priority is claimed under 35 USC 119. A copy of
PCT/US91/03388 is enclosed and the certified copy will be forwarded
as soon as it is received.

Minor amendments have been made to the specification. The
title has been changed to reflect the nature of the claimed
invention. Claims 1-5, 10-12 and 20-25 have been deleted. Claims

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6-9 and 17-19 have been amended. New claims 26-35 have been added. Basis for the new claims appears throughout the specification for example, claims 26, 27 and 33: page 10, line 30 to page 12, line 29, page 36, line 25 to page 39, line 20; claim 28, page 3, lines 10-22; claims 29 and 30, page 8, lines 28-33; claim 31, page 12, line 30 to page 13, line 10; claim 32, page 10, lines 4-18; claim 34, page 8, line 34 to page 9, line 4 and page 34, line 28 to page 35, line 8; and claim 35, page 28, line 24 to page 35, line 4. For convenience the claims as amended appear in Appendix A.

An Information Disclosure Statement, Form 1449 and authorization to charge the \$200.00 fee to Deposit Account No. 07-1060 accompanies this document. Copies of listed references which have not been previously submitted in parent applications are submitted herewith.

The objections and rejections are addressed below in order of their appearance in the office action.

Restriction Requirement

Applicants hereby confirm the election of Group II, claims 6-9 and 13-19. It is Applicants understanding that an election of species is not necessary because all species were searched and examined on the merits. Claims 1-5, 10-12 and 20-25 stand withdrawn from further consideration in this Application. Applicants hereby preserve their rights to pursue the subject matter contained in these withdrawn claims in one or more divisional applications filed pursuant to 35 U.S.C. 121. It is believed that the inventorship remains the same despite the withdrawal of non-elected claims.

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Rejections Based on 35 USC §112

The specification is objected to as failing to provide an adequate written description of the invention because of an error in referencing a SEQ ID for the bovine BMP-8 sequence in the last line of page 32. The specification has been amended, as suggested by the Examiner, indicating that the bovine BMP-8 sequence of Table 4 "corresponds to the sequence of SEQ ID NO:14 from amino acid position number 31 through position 142 wherein Met at position 97 is replaced with Leu, Asn at position 100 is replaced with His and Lys at position 137 is replaced with Arg."

The written description is also considered inadequate because where a SEQ ID NO: follows a reference to a Figure it is not clear whether the sequence of the SEQ ID is the equivalent of the entire Figure or the range of positions in the Figure because the position numbers in the Figures differ from the numbers in the SEQ ID. The specification has been amended to specifically reference the SEQ ID and position numbers for the SEQ ID. Reference to Figure 2 has been deleted. The specification as amended is considered to provide an adequate written description.

Claims 6, 13 and 17 are rejected as the disclosure is enabling only for claims limited to where the DNA of the claims encodes a protein having at least the sequence of amino acids that is encoded by nucleotide #430 through #843 of Figure 2. It is submitted that the claims as amended are enabled by the disclosure. Claim 6 as amended and claims 13 and 17 dependent thereon are directed to a DNA comprising three sequences (a), b) and c) which form part of the nucleotide sequence encoding BMP-8.

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Claims 17 and 18 are rejected as the disclosure is enabling only for claims limited wherein the protein recovered in step (b) is the one encoded by the coding regions of the DNA sequence of step (a) in both claims 17 and 18 and in claim 17 wherein the sequence is either that set forth in d) or e) or DNAs which encode the same protein(s) encoded by the DNAs of species d) or e). The claims have been amended to limit the protein recovered in step (b) to proteins encoded by the coding regions of the DNA of step (a). As discussed above, claim 6 (upon which claim 17 depends) has been amended to set forth three nucleotide sequences [a), b) and c)] which comprise part of the DNA sequence encoding BMP-8. It is therefore submitted that the claims as amended are enabled by the disclosure.

The specification is objected to as failing to provide an enabling disclosure for the claimed invention because the sequence of the DNA encoding BMP-8 of ATCC #75010 is not elsewhere disclosed and this DNA is claimed. The Examiner contends that the specification does not provide a repeatable method for obtaining ATCC #75010. Applicants submit that the description set forth on page 33, line 26 through page 34, line 27 provides a repeatable method for obtaining the DNA encoding BMP-8 of ATCC #75010. As suggested by the Examiner, a Declaration by the undersigned Attorney of record is submitted herewith to satisfy the deposit requirements. The Declaration states that ATCC #75010 and #75011 have been deposited under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public will be irrevocably removed upon the granting of a patent. It is therefore considered that the specification provides an enabling disclosure for claims 9 and 18.

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Claims 6-8, 13-15 and 19 are rejected as being indefinite because it is not clear whether the sequence of the SEQ ID NO: is the equivalent of the entire sequence of the Figure or the equivalent of the sequence corresponding to the range of positions in the Figure. Furthermore, it is noted by the Examiner that the position numbers of the Figures do not correspond with the SEQ ID. As recommended by the Examiner the claims have been amended to refer only to the SEQ ID and positions thereof. Claim 19 has been amended to reference a SEQ ID.

Rejections Based on 35 USC §101

Claims 6, 9, 13 and 16 are rejected for being directed to non-statutory subject matter. It is contended that the DNAs of species a), b) and c) of claim 6 and 9 and the host cells have the same characteristics and utility as that found in nature. The claims as amended are directed to isolated DNA sequences and are therefore considered to be distinguished from that found in nature.

In view of the above, it is submitted that the claims as amended are in condition for allowance. Reconsideration of the rejections and objections is requested.

Respectfully submitted,

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APPENDIX A

6. An isolated DNA sequence comprising the following sequences

a)

GTG CAC CTG CTG AAG CCG CAC GCG GTC CCC AAG GCG TGC TGC GCG CCC ACC
AAG CTG AGC GCC ACT TCC GTG CTC TAC TAC GAC AGC AGC AAC AAC GTC ATC
CTG CGC AAG CAC CGC AAC ATG GTG GTC CGC GCC TGC GGC TGC CAC (SEQ ID
NO: 7);

b)

GAC TGG GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA GGG GAG
TGC TCC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC ATC CTG
CAG TCC CTG (SEQ ID NO: 9); and

c)

GAC GTC CAC GGC TCC CAC GGC CGG CAG GTG
TGC CGT CGG CAC GAG CTG AGC TTC CAG GAC CTG GGC TGG CTG (SEQ ID NO:
11).

7. An isolated DNA sequence comprising the nucleotide sequence set
forth in SEQ ID NO:13 from nucleotide #8 to #850.

8. An isolated DNA sequence comprising the nucleotide sequence set
forth in SEQ ID NO: 13 from nucleotide #434 through #850.

9. An isolated DNA comprising the DNA sequence of ATCC #75010.

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13. A host cell transformed with a DNA of claim 6.

14. A host cell transformed with the DNA of claim 7.

15. A host cell transformed with the DNA of claim 8.

16. A host cell transformed with the DNA of claim 9.

17. A method comprising the steps of:

(a) culturing a cell transformed with a vector comprising a DNA sequence of claim 6 said DNA sequence in operative association with an expression control sequence therefor; and

(b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence.

18. A method comprising the steps of

(a) culturing a cell transformed with a vector comprising a DNA sequence of claim 9 in operative association w i t h a n expression control sequence therefor; and

(b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence.

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19. A method comprising the steps of:

(a) culturing a cell transformed with a vector comprising a DNA sequence comprising nucleotide #8 through #850 of SEQ ID NO:13 said DNA sequence in operative association with an expression control sequence therefore; and

(b) recovering, isolating, and purifying from said culture medium a protein characterized by an amino acid sequence comprising amino acid #4 to #142 of (SEQ ID NO:14).

26. A method comprising the steps of:

(a) culturing a cell transformed with a vector comprising a DNA sequence of claim 7 said DNA sequence in operative association with an expression control sequence therefor; and

(b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence.

27. A method comprising the steps of:

(a) culturing a cell transformed with a vector comprising a DNA sequence of claim 8 said DNA sequence in operative association with an expression control sequence therefor; and

(b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence.

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28. A DNA sequence encoding a protein comprising the following amino acid sequences:

a) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO: 1);

b) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2); and

c) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3).

29. The DNA of claim 6 wherein said protein has a molecular weight of 28,000-38,000 daltons and under reducing conditions a molecular weight of 14,000-20,000 daltons.

30. The DNA of claim 28 wherein said protein has a molecular weight of 28,000-38,000 daltons and under reducing conditions a molecular weight of 14,000-20,000 daltons.

31. A vector comprising the DNA of claim 28.

32. A DNA sequence which hybridizes under stringent conditions to the sequence of claim 28 and encodes a BMP-8 protein.

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33. A method comprising

a) culturing a cell transformed with a vector comprising a DNA of claim 28 in operative association with an expression control sequence therefor; and

b) recovering, isolating and purifying from said culture medium a BMP-8 characterized by the following sequences

i) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO: 1);

ii) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2); and

iii) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3);

34. A method for isolating a DNA sequence comprising

a) designing nucleotide probes based on the following amino acid sequences

i) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO: 1);

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ii) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-
Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2);

iii) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3);

b) screening a selected library with said probes; and
isolating said DNA sequence from said library said DNA encoding a
protein comprising the sequences set forth in i) through iii).

35. An isolated DNA sequence comprising the nucleotide sequence of
ATCC #75011.